Chapter 10

Drug Abuse-Induced Cardiac Arrhythmias: Mechanisms and Management

Sana Ouali, Omar Guermazi, Fatma Guermazi, Manel Ben Halima, Selim Boudiche, Nadim Khedher, Fathia Meghaieth, Abdeljalil Farhati, Noureddine Larbi and Mohamed Sami Mourali

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.76022

Abstract

Toxicomania is a worldwide emerging problem threatening young population. Several reports highlighted its hazardous cardiovascular effects. Sudden cardiac death secondary to cardiac arrhythmias is the most occupying issue. Different forms of cardiac rhythm disorders may be induced by illicit drug abuse according to the type of drug and the mechanism involved. In this review, we exposed the main ventricular and supraventricular arrhythmia complicating the common recreational drugs, and we explained their different mechanisms as well as the particularities of management.

Keywords: cardiac arrhythmias, illicit drugs, management, mechanism

1. Introduction

Toxicomania is a worldwide health and social problem. In 2015, the World Health Organization estimates that 255 millions of people are drug users and more than 10% of them have health disorders [1]. In Tunisia, the issue is more complicated as drug abuse begins at a very early age, affecting 4.2% of students aged between 15 and 17 years old [2]. This finding results in a chronic use and a more accumulation of these substances leading to serious health complications, among which cardiovascular ones are the most occupying

mainly acute coronary syndromes and rhythm disturbances resulting in more and more reported young's sudden cardiac deaths [3].

Most of the researches have focused on mental health effects and neurotoxicity of illicit drugs. Some of them were interested to cardiovascular dangers in general, and they were almost cases or series reports. The current review will focus on the topic of cardiac arrhythmias secondary to drug abuse in which we will explain their different mechanisms and principles of management.

2. Cocaine

This "white powder," extracted from coca leaves, is not only one of the oldest known stimulants but also the most known cardiotoxic illicit drug.

Several cases and series of sudden death, in the hours following cocaine consumption, were reported. The main likely cause is cocaine-induced arrhythmia [3].

Four mechanisms are implicated in the genesis of arrhythmia in case of cocaine intoxication: sodium channel blockade, potassium channel blockade, catecholamine excess, and finally myocardial infarction (MI) and myocarditis [4]. Recently, sinus bradycardia has been described as a result of chronic cocaine use [5–7] that may be related to a cocaine-induced desensitization of beta-adrenergic receptors [6].

The main measure for patients suffering from cocaine-induced arrhythmia is withholding the drug and referring to a detoxification center to prevent recurrent events. In addition, specific strategies should also be conducted according to the type of arrhythmia.

2.1. Sodium channel blockade

- Wide QRS tachycardia related to sodium channel blockade and reentry ventricular tachycardia

First, the blockade of fast inward sodium channels by cocaine is well described as a class IC effect according to the Vaughan-Williams classification of antiarrhythmic agents. Modulators of the effect of cocaine are increased in heart rate and decreased in pH which increases the degree of sodium channel blockade [8].

Electrocardiographic (ECG) manifestations mimic those of other sodium channel blockers, drugs and toxins, as tricyclic antidepressants. These manifestations depend on the degree of intoxication. In fact, early and minimal toxicity results in the impairment of conduction on the right side leading to a rightward axis deviation and QRS duration prolongation, and then, as toxicity increases, a right bundle branch block (RBBB) appears in the precordial leads (**Figure 1**). This pattern associated with sinus tachycardia, often shown in case of cocaine intoxication, may be confused with a true ventricular tachycardia resulting from a reentry or focal mechanism that can also complicate cocaine intoxication as reported in many series [4, 9, 10].

http://dx.doi.org/10.5772/intechopen.76022

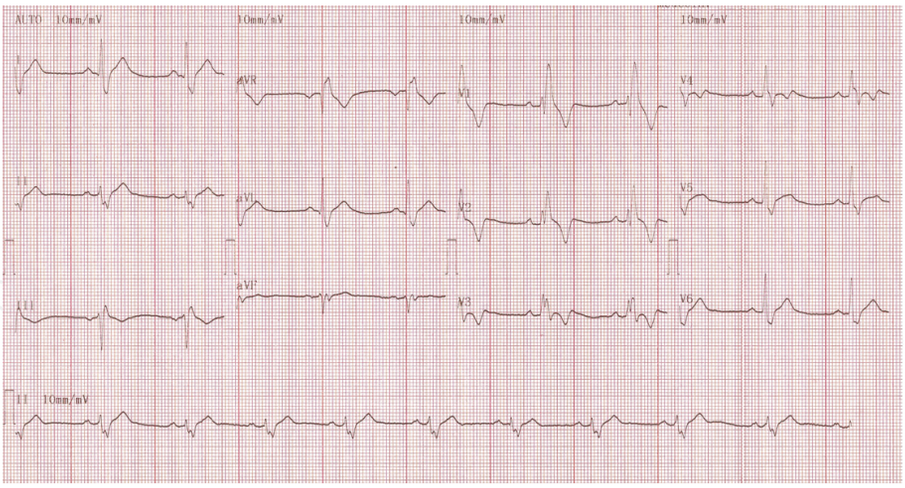

Figure 1. ECG performed after a wide QRS tachycardia cardioversion showing a complete right bundle branch block in a 38-year-old man with 10 years use of cocaine.

To manage this wide QRS tachycardia related to sodium channel blockade, general measures should rapidly be initiated. Oxygenation and ventilation should be optimized, and rapid cooling should be initiated when extreme hyperthermia is present. Sedation with a benzodiazepine is indicated to control behavior, to lower heart rate which may be sufficient to improve conduction and for its antianginal effects in patients with cocaine-associated acute coronary syndrome [4, 11].

This electrocardiographic manifestation, occurring in case of acute intoxication and mediated by pH decrease, is reversed by hypertonic sodium bicarbonate [8, 12, 13]. In case of persistence of this tachycardia with abnormal QRS prolongation, antiarrhythmic drugs should be administrated. Class IA and class IC antiarrhythmic drugs are classically contraindicated as they may potentiate QRS enlargement via a synergistic action on sodium channels. In contrast, lidocaine (class IB) can compete with cocaine for binding to the sodium channel, and it has a rapid offset responsible for the decrease in QRS duration. However, it was suggested that lidocaine exacerbated cocaine-associated seizures and arrhythmias as a result of similar effects on sodium channels [14]. Beta-blockers are contraindicated in case of cocaine intoxication as they exacerbate coronary vasospasm resulting in an increased risk of myocardial infarction [11]. No data exist concerning the efficacy of amiodarone in clinical cocaine intoxication [11].

- Brugada-like pattern

Moreover, a classic Brugada pattern has been noted in cocaine users, as seen with class IA antiarrhythmic drugs [15, 16]. It is quite likely that these patients express a sodium channel mutation described in association with Brugada abnormality and that the sodium channel blocking properties of cocaine made the patients' underlying physiological abnormality more evident [4]. Recently, El Mazloum et al. reported four cases of out-of-hospital cardiac arrest after acute cocaine intoxication associated with Brugada ECG patterns [17].

Cocaine abuse should be stopped. Mostly, ECG reverts toward normal as toxicity resolves [13]. Otherwise, sudden cardiac death risk should be evaluated, and implantable cardioverter defibrillator should be discussed in coordination with cardiac electrophysiologists.

2.2. Potassium channel blockade

Cocaine is known to block the rectifying potassium channels resulting in QT interval prolongation and hyperpolarization leading to early and late afterdepolarizations. If an afterdepolarization of significant magnitude occurs at a time when a critical number of cells can conduct an impulse, an ectopic beat can trigger a reentrant rhythm, and monomorphic ventricular tachycardia or torsades de pointes (TdP) occur [18–21].

Management of TdP and QT prolongation resulting from cocaine-associated potassium channel blockade is similar to those from other causes. In fact, for QT prolongation, electrolytic abnormalities, mainly hypokalemia and hypomagnesaemia, should be identified and rapidly corrected. Prophylactic magnesium is also suggested in patients with QT interval above 500 ms [4]. In case of TdP, magnesium, potassium replacement, and even overdrive are the main treatments. QT prolonging drugs should be withheld [4, 22].

2.3. Catecholamine excess

The common acute effect of cocaine is to block the presynaptic uptake of dopamine, norepinephrine, and epinephrine, resulting in an augmented level of these neurotransmitters at the postsynaptic terminal, producing an exaggerated catecholamine effect [23–25].

This produces sinus tachycardia, a very common finding in these patients, reentrant supraventricular tachycardia [26], and atrial fibrillation, noted in case and series reports [27].

Supportive care is generally sufficient to control sinus tachycardia. Sedation with benzodiazepine, oxygen, cooling, and volume resuscitation are the main measures. For reentrant supraventricular tachycardia, the use of a calcium channel blocker is often required. Finally, atrial fibrillation should be classically treated, using short-acting drugs as rhythm is generally controlled when toxicity resolves and avoiding β-blockers and class IA and IC antiarrhythmic drugs [4].

2.4. Myocardial infarction and myocarditis

The risk of myocardial infarction is multiplied by 24 within the next hour following cocaine consumption [28]. Cocaine-associated myocardial ischemia and infarction is a multifactorial process that results from increased demand, vasospasm, enhanced coagulation, impaired thrombolysis, and accelerated atherogenesis [29]. A catecholamine excess (trigger) induced by cocaine on such a vulnerable myocardium (substrate) may provoke the development of ventricular arrhythmias and sudden cardiac death.

In addition to myocardial infarction, scar-related macroreentrant ventricular tachycardia may also complicate cocaine-induced acute toxic myocarditis (**Figure 2**) as demonstrated in several case and series reports [30–32].

Figure 2. Cardiac magnetic resonance imaging revealing a late gadolinium enhancement (LGE) of the subepicardial layers of the septal and lateral walls of the left ventricle in a cocaine abuse man admitted for a ventricular tachycardia management.

When a cocaine-associated acute myocardial infarction is diagnosed, classical antithrombotic therapies should be administrated according to current guidelines, and primary PCI should be rapidly performed. Moreover, benzodiazepine should be initiated, and β-blockers have to be avoided because of the risk of further vasospasm [11, 33].

For scar-related reentry, as well as focal, ventricular tachycardia, management is based on classical measures and therapies according to current guidelines [34] with respect of the above-cited particularities and contraindications related to cocaine intoxication. In addition, implantable cardioverter defibrillator implantation should be deferred until the resolution of the acute episode [32, 34].

Besides these therapies, radiofrequency ablation using 3D mapping was described to be an effective therapy in 86% of drug refractory ventricular tachycardia related to cocaine use [10].

2.5. Sinus bradycardia and early repolarization pattern

Recent reports have demonstrated that chronic cocaine use is a strong predictor of sinus bradycardia compared with a matched group of nonusers and resulted in three- to seven-fold increased risk of sinus bradycardia [5–7]. Despite the presence of sinus bradycardia, all patients were able to augment their sinus rate with activity [6].

Sharma et al. have showed also that current cocaine dependence corresponds to an increased odd of demonstrating early repolarization by a factor of 4.92 [5].

Common physiological manifestations of cocaine are related to its adrenergic effects. However, with chronic exposure to cocaine, Franklin et al. have postulated that the mechanism of sinus bradycardia may be related to a cocaine-induced desensitization of beta-adrenergic receptors.

A blockage of the fast sodium current reduces sinus node automaticity, and results in bradycardia have also been evocated [6].

3. Cannabis

Because of its accessibility and legality of use in many countries, cannabis, also known as "marijuana" or "hashish," is the most consumed drug in Tunisia and all over the world [1, 2]. Cardiovascular complications of cannabis use rose from 1.1 to 3.6% between 2006 and 2010 among 9936 abusers according to the French Addictovigilance Network, most of them presenting with an acute coronary syndrome, while two patients had cardiac arrhythmia [35]. Due to its widespread use and of possible harmful cardiovascular impact reported in many case and series reports, cardiologists should be sensitized to detect its potential dangerous effects and be able to prevent and manage them properly.

Cannabis is rapidly absorbed through the lungs and less so with ingestion. The effects of the drug can last up to 6 hours with the onset of arrhythmias beginning anywhere from within a few minutes to a few hours of smoking and with a peak at 30 minutes [36].

Delta-9-tétrahydrocannabinol (Δ-9-THC), the active agent of cannabis, exercises its action via the cannabinoid system with its two receptors CB1 and CB2. This system induces modifications of the regulation of the autonomic nervous system leading to cardiovascular consequences and of central nervous system resulting in psychoneurological effects [37, 38].

Most published reports have focused on incidents of acute coronary syndromes and acute cerebrovascular and peripheral vascular events. However, an increasing number of case reports indicate an association between cannabis use and cardiac arrhythmias mainly atrial fibrillation (AF) and ventricular arrhythmias (**Figure 3**) [39]. Management and reversibility of these arrhythmias are similar to those induced by cocaine abuse and will not be re-explained in this chapter.

In fact, cannabis has a biphasic effect on the autonomic nervous system.

3.1. Increase in sympathetic activity

At low to moderate doses, THC leads to an increase in sympathetic activity causing sinus tachycardia with a rise of 20–100% of the heart rate, premature ventricular beats associated with increased cardiac output and hypertension [36]. The concept of sympathetic activation is supported by studies demonstrating an increased urinary excretion of epinephrine after THC use [40].

Atrial fibrillation is another complication of acute cannabis intoxication. A recent study focused on causes of atrial fibrillation in young people ≤45 years old. Among 88 patients, 22 of them, the atrial fibrillation was directly related to alcohol (86.4%), cannabis (13.6%), or cocaine abuse (4.5%) [41]. In a systematic review published in 2008, six reported cases were analyzed. In all instances, AF was of recent onset occurring shortly after marijuana smoking in young subjects. No patient had a structural heart disease, and only one had a precipitating factor (hypertension); all patients had a favorable outcome with no recurrence after cessation of marijuana smoking [42]. Of note, adrenergic stimulation and disturbances in atrial coronary or microvascular flow associated with marijuana smoking may facilitate AF development and perpetuation possibly because of increased pulmonary vein ectopy, enhanced atrial electrical remodeling, and increased dispersion of refractoriness [42]. It should also be stressed that although this adverse event seems to be quite "benign" in young healthy subjects, it is apparently more "malignant" in older patients having other risk factors for thromboembolism.

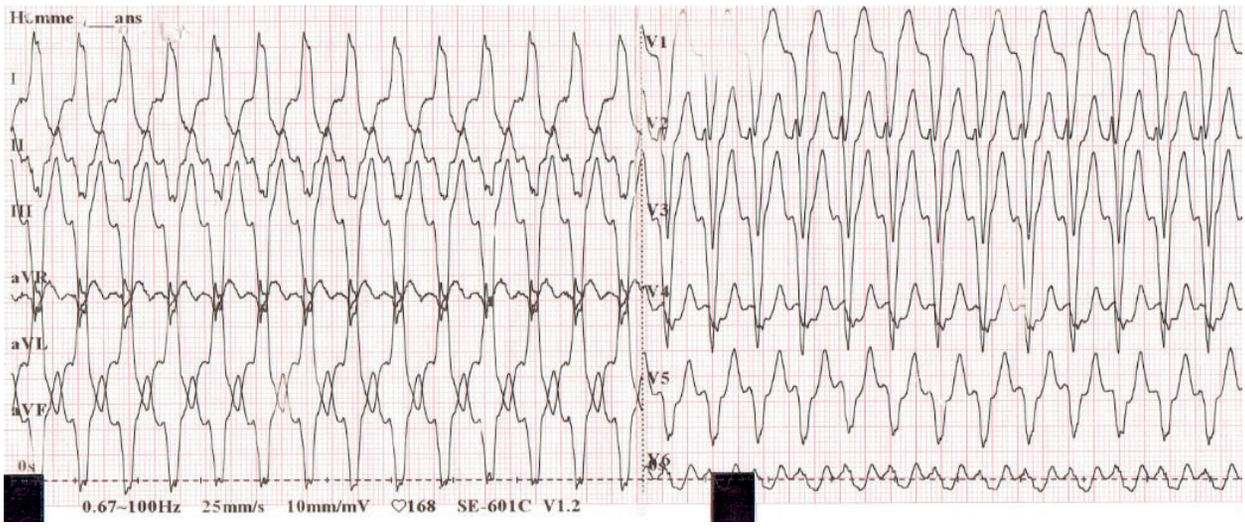

Figure 3. ECG showing a ventricular tachycardia at 170 beats/min with left bundle branch block pattern and left QRS axis in a 39-year-old man with a history of chronic cannabis use.

Finally, we should note that the burden of this problem is possibly underestimated given euphoric and neuropsychological effects of marijuana that may cover palpitations, possible occurrence of unnoticed short episodes of AF and because of social and legal reasons leading most users of illicit drugs to avoid seeking medical attention [43]. AF onset in young patients without structural heart disease should pay attention to an eventual illicit drug abuse. Its identification is very important because drug cessation will protect against AF recurrences.

3.2. Increase in parasympathetic activity

In contrast, at higher doses, parasympathetic activity is increased causing bradycardia and hypotension [36].

Bradyarrhythmias such as sinus bradycardia and higher-degree atrioventricular block have been reported. And, these conduction disturbances were reversible 72 hours after drug cessation [44].

The most described parasympathetic complication of cannabis abuse is vasovagal and postural syncope leading in some cases to sinus asystole. In a randomized controlled trial where 29 volunteers had participated, the effects of THC infusion and marijuana smoking when reclining and standing were studied. Both THC and marijuana-induced postural dizziness, with 28% reporting severe symptoms immediately after drug administration. The severe dizziness group showed the most marked postural drop in cerebral blood velocity and blood pressure and showed a drop in pulse rate after an initial increase during standing [45, 46].

3.3. Acute coronary syndrome

The risk of myocardial infarction (MI) is 4.8-fold increased in the first hour following marijuana use [47]. Urgent coronary angiography practiced in these victims of cannabis-induced MI may show angiographically normal coronary arteries supposing a spastic mechanism or an increased myocardial oxygen demand due to increased sympathetic activity. Coronary

arteries may also be very thrombotic with or without atherosclerotic plaque rupture. Finally, a no-flow or slow-flow with normal appearing epicardial vessels was reported as well [48]. Ventricular tachycardia and sudden cardiac death were reported as a complication of cannabis-induced MI [49].

3.4. Sodium channel blockade

A Brugada-like effect was reported to be associated to cannabis intoxication as described with cocaine abuse [50–52]. This ECG pattern is believed to be related to a partial sodium channel antagonist activity. The ST segment normalizes once the acute intoxication is resolved.

4. Amphetamines and derivatives: ecstasy and methamphetamines

These synthetic drugs are used for their psychostimulant effects. They had been first used by German army during the Second World War for these sought effects. Later, their cardiovascular dangers were revealed.

The main mechanism of action is an indirect sympathomimetic effect by releasing norepinephrine, dopamine, and serotonin from central and autonomic nervous system terminals, leading, as in cocaine intoxication, to an increase in the central and peripheral catecholamine concentrations [53].

High catecholamine levels are known to be cardiotoxic, causing vasospasm, tachycardia, and hypertension, leading to increased myocardial oxygen demand and myocyte necrosis and fibrosis [54].

The association of these stimulants and sudden cardiac death is well established. A recent histopathological study showed that among 100 methamphetamine poisoning-related deaths, 68% had cardiac lesions [55]. In this context, death can result either from lethal aortic dissection or from ventricular arrhythmia. This latter may complicate either type 1 and type 2 myocardial infarctions or methamphetamine-induced cardiomyopathy and is triggered by catecholamine excess [56]. Furthermore, according to an interesting recent study, among 230 amphetamine abuser patients, 43% presented with sinus tachycardia and 3.5% presented with cardiac arrhythmias: ventricular tachycardia, premature atrial beats, paroxysmal supraventricular tachycardia, and premature ventricular beats [57].

5. Heroine

Morphine and its semisynthetic analogue heroin are the most commonly used recreational narcotic drugs. Narcotic agents act centrally on the vasomotor center to increase parasympathetic and reduce sympathetic activity [48, 53]. These autonomic changes, combined with histamine release from mast cell degranulation, can result in bradycardia and hypotension [53]. Sinus bradycardia, benign atrioventricular block, and resulting atrial or ventricular automatic

ectopy and tachycardia were all reported. ECGs of 511 opioid addicts were analyzed. The main anomalies detected were sinus bradycardia, type-1 atrioventricular block, wandering atrial pacemaker, supraventricular and ventricular ectopic beats, and QT prolongation [58].

Methadone is another synthetic opioid used for the treatment of opioid addiction and for its analgesic effect. Methadone is responsible for QT prolongation and occurrence of torsade de pointes (TdP) especially when QT interval exceeds 500 ms. TdP should always be suspected in patients receiving methadone and presenting with syncope [59, 60]. Correction of predisposing factors as hypokalemia and hypomagnesemia is recommended, in case of prolonged QT and TdP. Magnesium perfusion is proposed, even in case of normal serum magnesium concentration. Alternative drugs can be used when corrected QT exceeds 500 ms [59].

6. Lysergic acid diethylamide and psilocybin

Lysergic acid diethylamide (LSD) and psilocybin "magic mushrooms" are commonly used hallucinogenic agents in developed countries. LSD is about 100 times more potent than psilocybin. Their mechanisms of action are complex and include agonist, partial agonist, and antagonist effects at various serotonin, dopaminergic, and adrenergic receptors. The adrenergic effects are usually mild and do not produce the profound sympathetic storms that can occur after taking cocaine, amphetamine, or ecstasy. Besides common sinus tachycardia, cardiovascular complications are rarely serious, although occasional instances of supraventricular tachyarrhythmias and myocardial infarction have been reported [61, 62].

7. Inhalent abuse

Inhalant abuse is the intentional inhalation of chemical vapors by sniffing, snorting, bagging, or huffing the substance to attain a euphoric effect. Spray paints, shoe polish, dust-off spray, glue, and lighter fluids are some products commonly abused by people. Glue sniffing has become a widespread form of inhalant abuse, usually among in adolescents and young adults.

Studies have indicated that about 20% of children in middle and high schools have experimented with inhalant substances [63]. These products are cheap, easily accessible at home, school, and workplace, and they are legal for all age groups (e.g., glue). Many common household products containing halogenated hydrocarbon like 1,1-difluoroethane (DFE) (known as Freon 152A used in refrigeration, dust-off spray, and airbrush painting) and toluene (used in glues) are abused by inhalation for euphoric effects [64].

Halogenated hydrocarbon abuse can cause a fatal malignant arrhythmia, termed "sudden sniffing death." Cardiotoxic effects have been described in human and in animal models [64].

Avella et al. [65] have demonstrated different levels in DFE tissues in the brain and heart, but the DFE level in the heart remained higher than the brain tissue after approximately

60-second post-DFE withdrawal. This may further result in abuser inhaling more DFE to sustain euphoric effect because central nervous system effects are reduced and thus lead to accumulation in the heart.

Recently, Joshi et al. [66] have showed that after multiple DFE doses in rats, severe arrhythmias such as ventricular fibrillation and ventricular tachycardia can be triggered. Exposure causes significant higher amount of epinephrine release than the control group [66] and an increased sensitivity of the myocardium to epinephrine [64, 67]. Furthermore, electrolyte imbalance, cardiac biomarkers, and oxidative stress markers were significantly affected and can cause damage to cardiomyocytes [66].

Alper et al. have demonstrated increase in QT duration, QT, and QTc dispersion in toluene users [68]. Toluene can cause inhibition of cardiac sodium currents like class I antiarrhythmics which can cause prolonged QT interval and have proarrhythmic effects [69].

Although the electrical function of the heart can be altered with acute exposure to hydrocarbons, prolonged use can cause structural damage that may also impede normal function [64].

Samples of cardiac muscle taken from inhalant abusers have shown interstitial edema, intramyocardial hemorrhages, contraction band necrosis, [70] edema, swollen and ruptured myofibrils, [71] and myocarditis and interstitial fibrosis [72].

In addition to arrhythmias, halogenated hydrocarbons have negative inotropic, dromotropic, and chronotropic effects on cardiac tissue [73]. Cases of atrioventricular conduction abnormality have been described in toluene intoxication [74].

8. Conclusion

Cardiac arrhythmia presents a potential dangerous complication leading to sudden cardiac death threatening young population. The most important mechanisms implicated in the genesis of arrhythmia in case of illicit drug intoxication are sodium channel blockade, potassium channel blockade, catecholamine excess, and finally myocardial infarction and myocarditis. Atrial fibrillation onset in young patients without structural heart disease should pay attention to an eventual illicit drug abuse. Its identification is very important because drug cessation will protect against atrial fibrillation recurrences. **Table 1** resumes physiopathological effects and main induced arrhythmias of commonly abused illicit drugs. Management should consist, first, on withholding drug intoxication with the collaboration of a detoxification center to prevent recurrent events, and, second, on common recommended measures as for the treatment of nondrug abuse arrhythmias with respect of some particularities and contraindications as in the case of cocaine intoxication. Thus, acute management of wide QRS tachycardia related to sodium channel blockade secondary to drug abuse, include oxygenation, sedation with benzodiazepine, and hypertonic sodium bicarbonate perfusion. Class IA and class IC antiarrhythmic drugs and beta-blockers are classically contraindicated. Electrical cardioversion is indicated in case of all hemodynamically unstable arrhythmias.

Illicit drug	Physiopathological effects	Induced cardiac arrhythmias
Cocaine	Sodium channel blockade	QRS enlargement with right bundle branch block
		Brugada-like syndrome
	Potassium channel blockade	QT prolongation
		Torsade de pointes
	Catecholamine excess	Sinus tachycardia
		Supraventricular tachycardia
	Myocardial infarction/myocarditis	Ventricular tachycardia/fibrillation
	Cocaine-induced desensitization of beta-adrenergic receptors	Sinus bradycardia
Cannabis	Increase in sympathetic activity	Sinus tachycardia
		Atrial fibrillation
		Premature ventricular beats
	Increase in parasympathetic activity	Sinus bradycardia
		Atrioventricular block
		Vasovagal and postural syncope
		Sinus asystole
	Myocardial infarction	Ventricular tachycardia/fibrillation
	Sodium channel blockade	Brugada-like syndrome
Methamphetamine and ecstasy	Catecholamine excess	Sinus tachycardia
		Supraventricular tachycardia
	Myocardial infarction	Ventricular tachycardia/fibrillation
Heroine and morphine methadone	Increase parasympathetic and reduce sympathetic activity	Sinus bradycardia
		Atrial or ventricular ectopy
	Potassium channel blockade	QT prolongation
		Torsade de pointes
LSD and psilocybin	Mild catecholamine excess	Sinus tachycardia

Table 1. Physiopathological effects and main induced arrhythmias of commonly abused illicit drugs.

Conflict of interest

None declared.

Author's contribution

All authors conceived, read, and approved the final manuscript.

Author details

Sana Ouali[1]*, Omar Guermazi[1], Fatma Guermazi[2], Manel Ben Halima[1], Selim Boudiche[1], Nadim Khedher[1], Fathia Meghaieth[1], Abdeljalil Farhati[1], Noureddine Larbi[1] and Mohamed Sami Mourali[1]

*Address all correspondence to: sanaouali@hotmail.fr

1 Cardiology Department, La Rabta Hospital, Tunis, Tunisia

2 Psychiatry Department, Hedi Chaker Hospital, Sfax, Tunisia

References

[1] UNODC. Executive Summary. Conclusion and Policy Implications of the World Drug Report [Internet]. 2017. Available from: https://www.unodc.org/wdr2017/field/Booklet_1_EXSUM.pdf

[2] De S, Nationale TE. Enquête MedSPAD en Tunisie: Résultats de l'enquête nationale. 2014. Available from: https://www.coe.int/T/DG3/Pompidou/Source/Activities/MedNET/activities2014/MedSPAD-TunisieFR-V5.pdf

[3] Fischbach P. The role of illicit drug use in sudden death in the young. Cardiology in the Young. 2017;**27**(S1):S75-S79

[4] Hoffman RS. Treatment of patients with cocaine-induced arrhythmias: Bringing the bench to the bedside. British Journal of Clinical Pharmacology. 2010;**69**(5):448-457

[5] Sharma J, Rathnayaka N, Green C, Moeller FG, Schmitz JM, Shoham D, Dougherty AH. Bradycardia as a marker of chronic cocaine use: A novel cardiovascular finding. Behavioral Medicine. 2016;**42**:1e8

[6] Franklin SM, Thihalolipavan S, Fontaine JM. Sinus bradycardia in habitual cocaine users. The American Journal of Cardiology. 2017;**119**(10):1611-1615

[7] Mahoney JJ 3rd, Haile CN, De La Garza R 2nd, Thakkar H, Newton TF. Electrocardiographic characteristics in individuals with cocaine use disorder. The American Journal on Addictions. 2017;**26**(3):221-227

[8] Wang RY. pH-dependent cocaine-induced cardiotoxicity. The American Journal of Emergency Medicine. 1999;**17**(4):364-369

[9] Afonso L, Mohammad T, Thatai D. Crack whips the heart: A review of the cardiovascular toxicity of cocaine. The American Journal of Cardiology. 2007;**100**(6):1040-1043

[10] Lakkireddy D, Kanmanthareddy A, Biria M, Madhu Reddy Y, Pillariesetti J, Mahapatra S, et al. Radiofrequency ablation of drug refractory ventricular tachycardia related to cocaine use: A feasibility, safety, and efficacy study. Journal of Cardiovascular Electrophysiology. 2014;**25**(7):739-746

[11] McCord J, Jneid H, Hollander JE, De Lemos JA, Cercek B, Hsue P, et al. Management of cocaine-associated chest pain and myocardial infarction: A scientific statement from the American Heart Association acute cardiac care committee of the council on clinical cardiology. Circulation. 2008;**117**(14):1897-1907

[12] Beckman KJ, Parker RB, Hariman RJ, Gallastegui JL, Javaid JI, Bauman JL. Hemodynamic and electrophysiological actions of cocaine. Effects of sodium bicarbonate as an antidote in dogs. Circulation. 1991;**83**(5):1799-1807

[13] Winecoff AP, Hariman RJ, Grawe JJ, Wang Y, Bauman JL. Reversal of the electrocardiographic effects of cocaine by lidocaine. Part 1. Comparison with sodium bicarbonate and quinidine. Pharmacotherapy. 1994;**14**(6):704-711

[14] Derlet RW, Albertson TE, Tharratt RS. Lidocaine potentiation of cocaine toxicity. Annals of Emergency Medicine. 1991;**20**(2):135-138

[15] Littmann L, Monroe MH, Svenson RH. Brugada-type electrocardiographic pattern induced by cocaine. Mayo Clinic Proceedings. 2000;**75**(8):845-849

[16] Bebarta VS, Summers S. Brugada electrocardiographic pattern induced by cocaine toxicity. Annals of Emergency Medicine. 2007;**49**(6):827-829

[17] El Mazloum R, Snenghi R, Zorzi A, Zilio F, Dorigo A, Montisci R, Corrado D, Montisci M. Out-of-hospital cardiac arrest after acute cocaine intoxication associated with Brugada ECG patterns: Insights into physiopathologic mechanisms and implications for therapy. International Journal of Cardiology. 2015;**195**:245-249

[18] Singh N, Singh HK, Singh PP, Khan IA. Cocaine-induced torsades de pointes in idiopathic long Q-T syndrome. American Journal of Therapeutics. 2001;**8**(4):299-302

[19] Kimura S, Bassett AL, Xi H, Myerburg RJ. Early afterdepolarizations and triggered activity induced by cocaine. A possible mechanism of cocaine arrhythmogenesis. Circulation. 1992;**85**(6):2227-2235

[20] Perera R, Kraebber A, Schwartz MJ. Prolonged QT interval and cocaine use. Journal of Electrocardiology. 1997;**30**(4):337-339

[21] Riaz K, McCullough PA. Fatal case of delayed repolarization due to cocaine abuse and global ischemia. Reviews in Cardiovascular Medicine. 2003;**4**(1):47-53

[22] Sorajja D, Munger TM, Shen W-K. Optimal antiarrhythmic drug therapy for electrical storm. The Journal of Biomedical Research. 2015;**29**(1):20-34

[23] Vongpatanasin W, Mansour Y, Chavoshan B, et al. Cocaine stimulates the human cardiovascular system via a central mechanism of action. Circulation. 1999;**100**:497-502

[24] Sofuoglu M, Nelson D, Babb DA, et al. Intravenous cocaine increases plasma epinephrine and norepinephrine in humans. Pharmacology, Biochemistry, and Behavior. 2001;**68**:455-459

[25] Lange RA, Hills LD. Cardiovascular complications of cocaine use. The New England Journal of Medicine. 2001;**345**:351-358

[26] Chakko S, Sepulveda S, Kessler KM, Sotomayor MC, Mash DC, Prineas RJ, et al. Frequency and type of electrocardiographic abnormalities in cocaine abusers (electrocardiogram in cocaine abuse). The American Journal of Cardiology. 1994;**74**(7):710-713

[27] Merigian KS. Cocaine-induced ventricular arrhythmias and rapid atrial fibrillation temporally related to naloxone administration. The American Journal of Emergency Medicine. 1993;**11**(1):96-97

[28] Mittleman MA, Mintzer D, Maclure M, Tofler GH, Sherwood JB, Muller JE. Triggering of myocardial infarction by cocaine. Circulation. 1999;**99**(21):2737-2741

[29] Talarico GP, Crosta ML, Giannico MB, Summaria F, Calò L, Patrizi R. Cocaine and coronary artery diseases: A systematic review of the literature. Journal of Cardiovascular Medicine (Hagerstown, Md.). 2017;**18**(5):291-294

[30] Rijal S, Cavalcante JL. Acute cocaine myocarditis: A word of caution. European Heart Journal. 2015;**36**(15):946

[31] Virmani R, Robinowitz M, Smialek JE, Smyth DF. Cardiovascular effects of cocaine: An autopsy study of 40 patients. American Heart Journal. 1988;**115**(5):1068-1076

[32] Caforio ALP, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: A position statement of the European Society of Cardiology Working Group on myocardial and pericardial diseases. European Heart Journal. 2013;**34**(33):2636-2648

[33] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P. ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presentingwith ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal. 2018;**39**(2):119-177

[34] Priori SG, Blomström-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. European Heart Journal. 2015;**36**(41):2793-2867

[35] Jouanjus E, Lapeyre-Mestre M, Micallef J. Cannabis use: Signal of increasing risk of serious cardiovascular disorders. Journal of the American Heart Association. 2014;**3**(2):1-7

[36] Johnson S, Domino EF. Some cardiovascular effects of marihuana smoking in normal volunteers. Clinical Pharmacology and Therapeutics. 1971;**12**(5):762-768

[37] Bouccin E, Eloye H, Hantson P. Complications vasculaires périphériques, cardiaques et cérébrales associeés à l'utilisation du cannabis. Annals of Clinical Toxicology. 2016;**28**(2):115-128

[38] Jones RT. Cardiovascular system effects of marijuana. Journal of Clinical Pharmacology. 2002;**42**:58S-63S

[39] Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: What cardiologists need to know. The American Journal of Cardiology. 2014;**113**(1):187-190

[40] Weiss JL, Watanabe AM, Lemberger L, Tamarkin NR, Cardon PV. Cardiovascular effects of delta-9-tetrahydrocannabinol in man. Clinical Pharmacology and Therapeutics. 1972;**13**(5):671-684

[41] Krishnamoorthy S, Lip GYH, Lane DA. Alcohol and illicit drug use as precipitants of atrial fibrillation in young adults: A case series and literature review. The American Journal of Medicine. 2009;**122**(9):851-856.e3

[42] Korantzopoulos P, Liu T, Papaioannides D, Li G, Goudevenos JA. Atrial fibrillation and marijuana smoking. International Journal of Clinical Practice. 2008;**62**(2):308-313

[43] Korantzopoulos P. Marijuana smoking is associated with atrial fibrillation. The American Journal of Cardiology. 2014;**113**(6):1085-1086

[44] Akins D, Awdeh MR. Marijuana and second-degree AV block. Southern Medical Journal. 1981;**74**(3):371-373

[45] Mathew RJ, Wilson WH, Davis R. Postural syncope after marijuana: A transcranial Doppler study of the hemodynamics. Pharmacology, Biochemistry, and Behavior. 2003;**75**(2):309-318

[46] Brancheau D, Blanco J, Gholkar G, Patel B, Machado C. Cannabis induced asystole. Journal of Electrocardiology. 2016;**49**(1):15-17

[47] Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. Circulation. 2001;**103**(23):2805-2809

[48] Harbaoui B. Complications cardiovasculaires de la toxicomanie. Archives des Maladies du Coeur et des Vaisseaux – Pratique. 2017;**256**:11-18

[49] Rezkalla SH, Sharma P, Kloner RA. Coronary no-flow and ventricular tachycardia associated with habitual marijuana use. Annals of Emergency Medicine. 2003;**42**(3):365-369

[50] Romero-Puche AJ, Trigueros-Ruiz N, Cerdan-Sanchez MC, Perez-Lorente F, Roldan D, Vicente-Vera T. Brugada electrocardiogram pattern induced by cannabis. Revista Española de Cardiología (English Edition). 2012;**65**(9):856-858

[51] Daccarett M, Freih M, Machado C. Acute cannabis intoxication mimicking brugada-like ST segment abnormalities. International Journal of Cardiology. 2007;**119**(2):235-236

[52] Pratap B, Korniyenko A. Toxic effects of marijuana on the cardiovascular system. Cardiovascular Toxicology. 2012;**12**(2):143-148

[53] Ghuran A, Nolan J. The cardiac complications of recreational drug use. The Western Journal of Medicine. 2000;**173**(6):412-415

[54] Karch's SBK. Pathology of Drug Abuse. 3rd ed. Boca Raton: CRC Press; 2002

[55] Akhgari M, Mobaraki H, Etemadi-Aleagha A. Histopathological study of cardiac lesions in methamphetamine poisoning-related deaths. Daru. 2017;**25**(1):5

[56] Kaye S, McKetin R, Duflou J, Darke S. Methamphetamine and cardiovascular pathology: A review of the evidence. Addiction. 2007;**102**(8):1204-1211

[57] Bazmi E, Mousavi F, Giahchin L, Mokhtari T, Behnoush B. Cardiovascular complications of acute amphetamine abuse: Cross-sectional study. Sultan Qaboos University Medical Journal. 2017;**17**(1):e31-e37

[58] Wallner C, Stöllberger C, Hlavin A, Finsterer J, Hager I, Hermann P. Electrocardiographic abnormalities in opiate addicts. Addiction. 2008;**103**(12):1987-1993

[59] Alinejad S, Kazemi T, Zamani N, Hoffman RS, Mehrpour O. A systematic review of the cardiotoxicity of methadone. EXCLI Journal. 2015;**14**:577-600

[60] Fanoe S, Hvidt C, Ege P, Jensen GB. Syncope and QT prolongation among patients treated with methadone for heroin dependence in the city of Copenhagen. Heart. 2007;**93**(9): 1051-1055

[61] Borowiak KS, Ciechanowski K, Waloszczyk P. Psilocybin mushroom (Psilocybe semilanceata) intoxication with myocardial infarction. Journal of Toxicology. Clinical Toxicology. 1998;**36**(1-2):47-49

[62] Ghuran A. Recreational drug misuse: Issues for the cardiologist. Heart. 2000;**83**(6):627-633

[63] U.S. Department of Health and Human Services. Monitoring the future survey release. Smoking among teenagers decreases sharply and increase in ecstasy use slows. U.S. Department of Health and Human Services HHS News; December 19; 2001. Retrieved July 3, 2003, from: www.nida.nih.gov/MedAdv/01/NR12-19.html

[64] Tormoehlen LM, Tekulve KJ, Nañagas KA. Hydrocarbon toxicity: A review. Clinical Toxicology (Philadelphia, Pa.). 2014;**52**:479-489

[65] Avella J, Kunaparaju N, Kumar S, et al. Uptake and distribution of the abused inhalant 1,1-difluoroethane in the rat. Journal of Analytical Toxicology. 2010;**34**:381-388

[66] Joshi K, Barletta M, Wurpel J. Cardiotoxic (Arrhythmogenic) effects of 1,1-difluoroethane due to electrolyte imbalance and cardiomyocyte damage. The American Journal of Forensic Medicine and Pathology. 2017;**38**(2):115-125

[67] Himmel HM. Mechanisms involved in cardiac sensitization by volatile anesthetics: General applicability to halogenated hydrocarbons? Critical Reviews in Toxicology. 2008;**38**:773-803

[68] Alper AT, Akyol A, Hasdemir H, Nurkalem Z, Güler O, Güvenç TS, Erdinler I, Cakmak N, Eksik A, Gürkan K. Glue (toluene) abuse: Increased QT dispersion and relation with unexplained syncope. Inhalation Toxicology. 2008;**20**(1):37-41

[69] Cruz SL, Orta-Salazar G, Gauthereau MY, et al. Inhibition of cardiac sodium currents by toluene exposure. British Journal of Pharmacology. 2003;**140**:653-660

[70] Sakai K, Maruyama-Maebashi K, Takatsu A, Fukui K, Nagai T, Aoyagi M, et al. Sudden death involving inhalation of 1,1-difluoroethane (HFC-152a) with spray cleaner: Three case reports. Forensic Science International. 2011;**206**:e58-e61

[71] Banathy LJ, Chan LT. Fatality caused by inhalation of "liquid paper" correction fluid. The Medical Journal of Australia. 1983;**2**(12):606

[72] Wiseman MN, Banim S. "Glue sniffer's" heart? British Medical Journal (Clinical Research Ed.). 1987;**294**(6574):739

[73] Muller SP, Wolna P, Wunscher U, Pankow D. Cardiotoxicity of chlorodibromomethane and trichloromethane in rats and isolated rat cardiac myocytes. Archives of Toxicology. 1997;**71**:766-777

[74] Tsao JH, Hu YH, How CK, Chern CH, Hung-Tsang Yen D, Huang CI. Atrioventricular conduction abnormality and hyperchloremic metabolic acidosis in toluene sniffing. Journal of the Formosan Medical Association. 2011;**110**(10):652-654

IntechOpen